REMARKS

The following remarks are in response to the Examiner's Office Action mailed on March 24, 2004. Claims 20 and 32-46 have been canceled without prejudice. Claims 3-8, 10, 11, 13-17 and 47-50 have been withdrawn. Claims 1, 24, 26, 27 and 29 been amended. Claims 1, 2, 9, 12, 18, 19 and 21-31 are pending.

I. Election Restriction

The Examiner withdrew from further consideration of claims 25-28 and 47-50 as being drawn to a nonelected invention and species. Applicants respectfully traverse based on the following reason.

Pursuant to 37 C.F.R. §1.145, "[i]f, after an office action on an application, the applicant presents claims directed to an invention **distinct from and independent of** the invention previously claimed, the applicant will be required to restrict the claims to the invention previously claimed if the amendment is entered, subject to reconsideration and review as provided in 1.143 and 1.144". Emphasis added.

Since claims 25-28 and 47-50 are **dependent from** claim 1 that specifies the invention that Applicants elected in the Amendment filed in response to the Examiner's Restriction Requirement, these claims are not the type of claims required by 37 C.F.R. §1.145 to be reconsidered and reviewed under 37 C.F.R. §§1.143 and 1.144. Withdrawn of the restriction requirement is therefore respectfully requested.

II. Specification

The Examiner objected to the abstract for being too long. Applicants replace the abstract with a new one shown on page 2 of this Amendment. Withdrawal of the objection is therefore respectfully requested.

III. Rejection Under 35 U.S.C. 112, First Paragraph

The Examiner has rejected claims 1-24 and 29-31 under 35 U.S.C. §112, first paragraph for failing to comply with the written description requirement.

Specifically, the Examiner alleges that the specification fails to teach how to make and use the instantly claimed method of identifying multiple activated transcription factors with any cis element, promoter and reporter sequences. Applicants respectfully traverse the Examiner's rejection based on the following reasons.

Applicants respectfully direct the Examiner's attention to pages 12-15, a section under "DETAILED DESCRIPTION OF THE INVENTION", and Figures 1A, 1B, and 2. The present invention relates to rapid and efficient methods for the parallel identification of multiple different activated transcription factors in a biological sample. To identify the transcription factors in parallel, cis elements that are known to bind to different transcription factors are incorporated into a library of nucleic acid constructs. Meanwhile, a different reporter sequence is also incorporated into each member of the library to serve as a unique tag for each of the cis-element. Figure 2 shows examples of the cis element (e.g., SEQ ID NO: 1) and examples of the reporter sequence (e.g., SEQ ID NO: 31) corresponding to the cis element listed in the column to its left side. Upon binding of the transcription factor to the cis element and activation of transcription, the cis element and its accompanying reporter sequence are transcribed. Because each cis element is tagged with a different reporter sequence, identification of the reporter sequence will lead to identification of the activated transcription factor that binds to the cis element. Page 12, lines 22-31. Figure 1A illustrates an embodiment of the invention in which mRNA of the transcribed reporter sequences in the construct is isolated and reverse transcribed into cDNA which is then characterized. Characterization of the cDNA translates into the identification of the cis element, which in turn results in identification of the corresponding transcription factor. Page 14, lines 11-16. The specification further teaches how to construct the cis element – reporter construct on pages 15-19, and how to detect activated transcription factor on pages 19-28.

In view of the detailed description and ample examples provided in the specification, Applicants submit that the claimed invention is adequately described to convey to one skilled in the relevant art that the inventors at the time the application was filed had possession of the claimed invention under 35 U.S.C. §112, First Paragraph. Withdrawal of this ground of rejection is respectfully requested.

IV. Rejection Under 35 U.S.C. 112, Second Paragraph

The Examiner has rejected claims 1-24 and 29-31 under 35 U.S.C. 112, Second Paragraph as being indefinite. Applicants cancel claim 20 and amend claims 1, 24, 26, 27 and 29 as suggested by the Examiner and therefore respectfully request withdrawal of the rejection under 35 U.S.C. §112, Second Paragraph.

V. Obviousness-Type Double Patenting

Claims 1-24 and 29-31 are rejected under the judicially created doctrine of obviousness type double patenting as being unpatentable over claims 1-19 of U.S. Patent No: 6,696,256 ('256 patent). Claims 1-24 and 29-31 are also provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1 and 34-49 of co-pending applications Nos: 09/947,274 ('274 application) and 09/877,705 ('705 application). Applicants respectfully traverse the Examiner's rejection based on the following reasons.

Pursuant to MPEP §804(II)(B)(1), for any obviousness-type double patenting rejection one must examine: (A) the differences between **the inventions defined by the conflicting claims** - a claim in the patent compared to a claim in the application; and (B) the reasons why a person of ordinary skill in the art would conclude that the invention defined in the claim in issue is an obvious variation of the invention defined in a claim in the patent. When considering whether the invention defined in a claim of an application is an obvious variation of the invention defined in the claim of a patent, **the disclosure of the patent may not be used as prior art.** Emphasis added.

> The basis of the Examiner's rejection is as follows:
>
> The '256 Patent and the instant application are drawn to the same method of identifying multiple different tfs in a cell sample **using the same components therein, i.e., a transcription factor that includes a cis element and reporter sequence**.

Office Action, page 10, emphasis added.

Applicants respectfully point out that 1) a transcription factor does not include a cis element and a reporter sequence but binds to a cis element, instead; and 2) the library of

transcription factor probes recited in the claims of '256 patent, '274 application and '705 application are distinctively different from the library of constructs. Independent claim 1 recites a construct comprising a cis element and a reporter sequence which is expressed to produce an mRNA product. In contrast, the transcription factor probe in the claims of '256 patent, '274 application and '705 application forms a protein-nucleic acid complex which is further characterized. None of the claims in these patent and applications recites reporter sequences which are transcribed into mRNA products.

In view of these structural and functional differences between the pending claims of the instant application and the claims of '256 patent, '274 application and '705 application, Applicants submit that pending claims of the instant application are patentably distinct from those in cited patent and applications. Withdrawal of the obviousness-type double patenting rejection is therefore respectfully requested.

VI. Rejection Under 35 U.S.C. 103(a)

1. Claims 1-24 and 29

The Examiner has rejected claims 1-24 and 29 under 35 U.S.C. 103(a) as being unpatentable over Kamb (U.S. Pat. No. 6,579,675) in view of Mauro et al. (WO 01/555371) and Kauffman et al. (U.S. Pat. No. 6,413,723).

Independent claim 1 as amended specifies a method for identifying multiple different activated transcription factors in a cell sample. The method includes transducing or transfecting a cell sample with **a library of constructs**. **Each construct** includes a different **cis element** sequence to which a specific transcription factor is known to bind, **a promoter sequence** 3' relative to the cis element sequence, and a different **reporter sequence** 3' relative to the promoter sequence. Upon binding of a transcription factor in the cell sample to one of the cis elements, which activates transcription, the reporter sequence is transcribed. Determination of the transcribed reporter sequence identifies the cis element contained in the same construct as the reporter sequence, thereby identifying the corresponding transcription factor that binds to the cis element.

> The Examiner characterizes the primary reference Kamb as teaching the following:
>
> Kamb et al discloses at col. 3, lines 5-57 a method of identifying proteins (activated transcription factors as claimed) in a cell sample comprising introducing an **expression library** of perturbagens comprising e.g., of fragmented gDNA, random cDNA or synthetic DNA of random sequences **engineered to contain a reporter gene under the control of a cell type specific cis regulatory sequence** (col. 12, lines 17—26) in the cells.

Office Action, page 12, 3rd paragraph, emphasis added

Contrary to the Examiner's characterization of the reference, Kamb describes a method for identifying perturbagen that regulates traits of interest using a completely different approach than the present invention. Column 3, lines 6-10. Specifically, a perturbagen **expression library** that comprises of fragmented gDNA, random cDNA or synthetic DNA of random sequences is constructed and **introduced** into **host cells engineered to contain a reporter gene under the control of a cell-type specific cis regulatory sequence**. Column 12, lines 17-22. As further evidenced in the EXAMPLE section, a yeast gDNA perturbagen library was constructed and introduced into separate cell populations containing the a-factor-responsive GFP vector (i.e., the reporter gene). Column 20, lines 14-16. Clearly, the expression library in Kamb does NOT contain a reporter gene. Instead, it is the host cell into which the expression vector is introduced contains a reporter gene under the control of a cis regulatory sequence. Thus, Kamb fails to the claimed method wherein a library of constructs each comprising a cis element and a reporter sequence is introduced to a cell sample.

Neither Mauro et al. nor Kauffman teaches or suggests the claimed method. The Examiner asserts that Mauro et al. teaches a method of **identifying a transcription factor** in a sample by introducing into the cell sample a **random** library constructs comprising of a promoter with a cis-element and a plurality of reporter sequences. In fact, Mauro et al teaches a method of identifying **oligonucleotides** having transcriptional or translational activity, not transcription factors (which are proteins). *See* Abstract and Summary of Invention, page 4, lines 18-19. To do so, a random synthetic oligonucleotide sequence that **is based on, but different from** a **known oligonucleotide** such as **a known transcriptional regulatory element**, is incorporated into an expression vector. Page 5, lines 18-22. Thus, Mauro et al. fails to teach the claimed

method of identifying multiple transcription factors by using a construct comprising a cis element that is known to bind to a transcription factor, such as the one listed in the table shown in Figure 2. Further, Kaufmann merely discloses a random population of oligonucleotides of low diversity, which, similar to Mauro, fails to teach the claimed method.

In view of the failure of the cited reference to teach or suggest the claimed invention, a prima facie case of obviousness has not been established under 35 U.S.C. §103(a). Withdrawal of this ground of rejection is therefore respectfully requested.

2. Claims 30 and 31

The Examiner has rejected claims 30 and 31 under 35 U.S.C. §103(a) as being unpatentable over Kamb in view of Mauro et al. and further in view of Weismann et al. (U.S. Patent No: 6,066,452).

As discussed in detail above, neither Kamb nor Mauro teaches or suggests the claimed method wherein a library of constructs each comprising a cis element and a reporter sequence is introduced to a cell sample and the cis element is known to bind to a transcription factor.

On the other hand, Weissman et al discloses a method for identifying **new pairs** of transcription factor-DNA binding sites by using **a library of nucleic acid probes** with **randomized** sequences. Column 2, lines 4-15. Specifically, Weissman et al. teaches using a library of oligonucleotide probes having randomized sequences –NNNNNNNNN- (column 12, line 49) to "fish out" transcription factors that can bind to any of the randomized DNA sequences (column 13, Table 3). Thus, Weissman also not only fails to teach the claimed method of introducing to a cell sample a library of constructs each comprising a different cis element known to bind a transcription factor, a promoter and a reporter gene, but also fails to teach expressing the reporter sequence and isolating the mRNA products as specified in claim 1.

In view of the failure of the cited reference to teach or suggest the claimed invention, a prima facie case of obviousness has not been established under 35 U.S.C. §103(a). Withdrawal of this ground of rejection is therefore respectfully requested.

CONCLUSION

In light of the remarks and arguments set forth above, Applicants earnestly believe that they are entitled to a letters patent, and respectfully solicit the Examiner to expedite prosecution of this patent application to issuance. Should the Examiner have any questions, the Examiner is encouraged to telephone the undersigned.

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Respectfully submitted,

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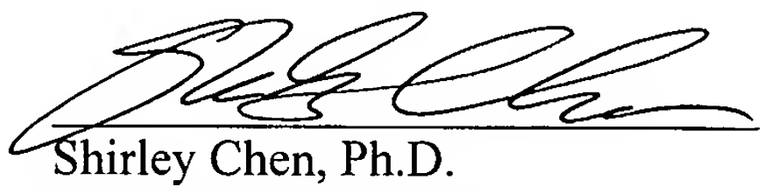
By: 
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